increased mortality from tumor in recipients of β7−/− donor T cells, suggesting preservation of any graft-versus-tumor activity. We are currently performing further studies to look at histopathology of GVHD target organs and to analyze T cell infiltrates in GVHD target organs. In summary, β7−/− donor T cells as compared to wild type donor T cells cause less GVHD morbidity and mortality. Our data suggest that strategies that interfere with the β7 integrin have clinical potential to alleviate or prevent GVHD while preserving GVT activity.

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DETERMINANTS OF ANTILEUKEMIA EFFECTS OF ALLOGENEIC NATURAL KILLER CELLS

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In HLA-nonidentical bone marrow transplantation, we sought to determine the characteristics of donor NK cells, recipient leukemia cells, and the cytokine environment that predict the antileukemia effects of allogeneic NK cells. We found that the risk of leukemia relapse in a prospective cohort of 36 pediatric patients was best predicted by a model taking into consideration the presence of inhibitory killer-cell immunoglobulin-like receptors (KIRs) on the donor's NK cells and the absence of corresponding KIR ligand in the recipient's HLA repertoire (a receptor-ligand model). The risk of relapse was prognosticated less precisely by the Perugia donor-recipient KIR ligand-ligand mismatch model or by a natural cytotoxicity model. In contrast to the Perugia model, we found that the new receptor-ligand model was accurate when analysis was applied to patients with lymphoid malignancy. These findings corroborate our observations that the recipient's KIR repertoire, which was derived from highly purified HLA-disparate $CD34^+$ cells, always resumed a donor-specific pattern within 3 months of transplantation but did not correlate evidently with either the donor or recipient ligand repertoire. In an in vitro assay and an in vivo mouse model, human NK-cell cytotoxicity toward human leukemia cells with 11q23 chromosomal rearrangement increased with the number of receptor-ligand mismatch pairs or prestimulation with IL-12 and IL-18. These findings provide new insights into the determinants of antileukemia effects of allogeneic NK cells and therapeutic strategies.

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PROTEINURIA RELATED TO CHRONIC GRAFT-VERSUS-HOST DISEASE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Proteinuria related to chronic graft-versus-host disease (GVHD) is an uncommon manifestation post allogeneic stem cell transplantation (SCT). Several papers have recently addressed this issue. We report our experience in four allogeneic SCT. Between April-2001 to November-2002, four women received full matched sibling allografts for aplastic anemia (n = 2), RAEB-I (n = 1) and CML (n = 1). Median age 28 years (range 20-40). Median time from diagnosis to transplantation was 7 months (range 6-12). Conditioning regimen for aplastic anemia was: antilymphocyte globulin + cyclophosphamide , for RAEB-I: total body irradiation + cyclophosphamide, finally for CML: Busulfan p.o.+ cyclophosphamide. GVHD prophylaxys were given with cyclosporine and methrothexate . All patient engrafted, neutrophils engraftment at median of 10 days (range 9-11), non-platelets failure was observed. Acute GVHD was observed in three cases. Proteinuria during chronic GVHD exacerbation was developed at a median time of 12 months (range 10-18) post peripheral blood SCT. None of them developed renal failure neither hypertension. Edema and hypoalbuminemia was observed in several degrees. During chronic GVHD exacerbation, one patient developed lung GVHD, another polimyositis and two showed positivity to cytomegalovirus (CMV) antigenemia with extensive GVHD manifestations. Two of them developed proteinuria at nephrotic range. Renal biopsies were carried out showing: diffuse proliferative glomerulonephritis, membranous nephropathy with IgG , C3 and Lambda immune complex deposit (F/24) and focal interstitial atrophy and fibrosis, mild membranous nephropathy with C1q immune complex deposit (F/32). Prednisone based therapy with mycophenolate mofetil (n = 3) and cyclosporine (n = 1) combined with gancyclovir for CMV antigenemia, resulted in renal function stabilization and gradual proteinuria decreases. Currently all of the patients are still alive in complete remission without transfusion and chronic GHVD improvement. Our data suggest that the kidney may be a target organ in chronic GVHD with immune complex-mediated disease. Finally we recommend that proteinuria has to be tested under chronic GVHD exacerbations.

Table. *Patients Characteristics*

Sex/age	Primary Disease	Acute-GVHD	Chronic-GVHD	Initial Proteinuria (mg/24 h)	Proteinuria Post-SCT (months)
F/32	Aplastic anemia	II	Extensive	1248	18
F/40	Aplastic anemia	I	Extensive	466	15
F/24	RAEB I	II	Extensive	2294	10
F/20	CML Ph + ICP	none	Extensive	427	10

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TACROLIMUS IN COMBINATION WITH STEROIDS FOR THE TREATMENT OF CHRONIC GVHD

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Background: Tacrolimus is an effective drug for the treatment of graft-versus-host disease (GvHD). Recent studies have shown that tacrolimus may be better than cyclosporine for the prevention of GvHD. Other studies have shown that it was an effective salvage therapy for chronic GvHD, even in patients previously treated with cyclosporine. We report the efficacy of tacrolimus/steroids as frontline treatment of chronic GvHD. Methods: Retrospective evaluation of 104 patients who had an allogeneic HSCT between 1/99-12/00 treated with a combination of tacrolimus and steroids for chronic GvHD. Results: Among the 104 patients (M/F = 74/30), 64 had HLA-matched sibling, 36 matched unrelated and 4 mismatched related transplants. The underlying diseases included: AML/MDS = 33, CML/MPD = 25, Lymphoma = 28, ALL/CLL = 11, Myeloma = 4, others = 3. Chronic GvHD was de novo in 33 cases, relapsing in 59 and progressive in 12 patients. The disease was limited in 20 and extensive in 84 patients. In 79% cases ≥2 organs were involved (skin = 84, liver = 43, mouth = 40, GI = 37, eyes = 24, lung = 13, hematologic = 13, musculoskeletal = 2, other = 5). GvHD was documented by histology in 56/81 cases where biopsy examination was performed at the time or following diagnosis of chronic GvHD. The overall CR/PR rate to tacrolimus/steroids was 72% (n = 75). Twenty-eight (27%) patients developed did not respond (NR) or developed progressive disease (PD). The majority of responses were seen in skin (n = 56, 79%) and oral (n = 19, 76%) chronic GvHD. Most failures were seen in patients with GVHD of the eye (n = 5, 50%), GI tract (n = 11, 41%) and liver (n = 9, 29%). In 49 cases (47%) salvage immunosuppression was required after first line treatment with tacrolimus/steroids. The majority of patients (n = 34, 69%) responded to salvage therapy. Fifty patients (48%) in this series died with an overall cGvHD-related mortality of 34%. Conclusions: Responses